REMARKS

Examination of claims 1, 3-7, 10, 11, 14-20, 22-24, and 28-30 is reported in the present Office Action. Claims 14-16, 19, 29, and 30 were rejected under 35 U.S.C. § 112, second paragraph; claim 17 was rejected under 35 U.S.C. § 101; claims 1, 3-7, 10, 11, 14, 15, 18-20, 22-24, and 28-30 were rejected under 35 U.S.C. § 102(b); and claims 1, 3-7, 10, 11, 14-20, 22-24, and 28-30 were rejected under 35 U.S.C. § 102(e). Each of the rejections is addressed as follows.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 14-16, 19, 29, and 30 were rejected under 35 U.S.C. § 112, second paragraph on several grounds, which are addressed as follows.

Claims 14-16 were rejected for reciting method steps in the passive voice. This rejection has been overcome by the present amendment to claims 14-16, in which these claims have been amended to recite steps in a positive manner, as was suggested in the Office Action.

Claim 19 was rejected as being indefinite for depending from claim 1 and reciting the phrase "further consisting essentially of an additional Helicobacter antigen." Applicant respectfully disagrees with this rejection but, in the interest of expediting prosecution, has amended claim 19 so that it no longer depends from claim 1.

Claims 29 and 30 were rejected on the basis that it is not clear whether the additional Helicobacter antigen (claim 29) or adjuvant (claim 30) impact the appearance of the molecular weight of the claimed protein when fractionated by SDS PAGE. Claim 30 has been canceled. With respect to claim 29, this rejection has been met by the present amendment to this claim, by which the claim now clearly states that the claimed composition includes two separate

components: (i) a polypeptide that appears to be on the order of 54 kDa when fractionated by SDS-PAGE, and (ii) an additional Helicobacter polypeptide antigen. Applicants thus respectfully request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 101

Claim 17 was rejected under § 101 on the basis that the claimed protein may exist in nature in the form that is claimed. This rejection has been met by the present amendment to claim 17, which now specifies that the protein is isolated. Applicant thus respectfully requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1, 3-7, 10, 11, 14-20, 22-24, and 28-30 were rejected under 35 U.S.C. §§ 102(b) and (e) over several references[1] that describe fractionation of Helicobacter protein preparations on gels, and detection of bands on these gels that have sizes that are similar to the sizes of the proteins now claimed. Some of these references, as well as an additional reference,[2] were also cited for describing antibodies that recognize proteins having these or similar sizes. None of the cited references anticipate the compositions now claimed. In particular, as is noted above, the claims are now drawn to compositions that consist of particular proteins in a pharmaceutically acceptable form or antibodies that recognize these proteins. The Helicobacter protein

[1] Husson et al., Infection and Immunity 61:2694-2697, 1993
Calenoff, U.S. Patent No. 5,567,594
Bölin et al., Journal of Clinical Microbiology 33:381-384, 1995
Doig et al., Infection and Immunity 62:4526-4533, 1994
Alemohammad, U.S. Patent No. 5,262,156
Pronovost et al., U.S. Patent No. 5,846,751
Pronovost et al., U.S. Patent No. 5,814,455
[2] Ruiz et al., WO 94/06474

preparations of the cited references each include numerous proteins and, thus, even if they were found to include the proteins of the present claims, they do not "consist of" these proteins. In addition, even if these proteins were found to be present in the gels on which the protein preparations of the cited references were fractionated, their presence in such gels cannot be considered to be in a "pharmaceutically acceptable form," as is also required by the present claims. In addition, the antibodies described in the cited references are present in mixtures of antibodies, and thus are not present in compositions that "consist of" these antibodies, as is required by the present claims. Thus, the rejections of the present claims over the references listed in the footnotes should be withdrawn.

Claims 1, 19, 20, 29, and 30 were rejected under § 102(b) as being anticipated by Ferrero (Proc. Natl. Acad. Sci. U.S.A. 92:6499-6503, 1995). The Office cites this reference for teaching a composition containing Helicobacter urease and a 54 kDa heat shock protein, as well as a composition containing a 54 kDa heat shock protein and cholera toxin. This rejection can now be withdrawn, because claim 1 has been amended to specify a composition that consists of certain antigens, none of which is 54 kDa; claim 19 is now drawn to a composition that consists of certain antigens, none of which is 54 kDa, and an additional Helicobacter polypeptide antigen; claim 20 is now drawn to a composition that consists of certain antigens, none of which is 54 kDa, and a urease antigen; and claim 30 has been canceled, without prejudice.

Regarding claim 29, applicant notes that Ferrero does not describe a composition that consists of a 54 kDa protein and urease in pharmaceutically acceptable form, as is required by this claim. Rather, the passage referred to by the Office as describing such a composition (page 6499, sentence bridging columns 1 and 2) merely notes that urease and a 54 kDa protein have been observed to be associated with one another, not that such proteins were together in a

composition, in a pharmaceutically acceptable form. Applicant thus requests that the rejection over the Ferrero reference be withdrawn.

For completion, applicant notes that the rejections under § 102 in this case were made over references describing the detection of polypeptides that may be somewhat close in size to those of the present claims. In making these rejections, the Office has stated that applicant bears the burden of proving that their proteins do not correspond to those of the cited references, because the Office does not have facilities for comparing the claimed proteins with those of the prior art. Applicant respectfully disagrees.

In order for the burden to shift to the applicant in such a rejection, the Office must first provide rationale or evidence tending to show inherency, which has not been done in this case. In particular, the M.P.E.P., § 2112, states on this point that "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish inherency of that result or characteristic" (citation omitted). This section of the M.P.E.P. also states that "to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient" (citation omitted). As is discussed further below, the Office has not met this standard in making the present rejection and, thus, the burden has not shifted to applicant to prove that their claimed invention differs from the teachings of the prior art. The Office has not shown that the proteins of the present claims are necessarily present in the gels of the cited references, and any assertion that the probabilities or possibilities might tend to point in this direction would not suffice in establishing a proper rejection.

The Office has cited references showing detection of Helicobacter proteins that are somewhat close in size to the proteins and polypeptides of the present claims, and that is all. Evidence has not, for example, been provided that would indicate that the methods recited in applicant's claims would yield the same proteins as those on the gels of the cited references. Mere detection of a protein in a somewhat similar size range does not meet this standard for several reasons. For example, it is known that bacterial outer membrane proteins include a large number of proteins, greatly exceeding the number of bands that can be detected on an SDS-PAGE gel. As a consequence, there can be no certainty that a band on an analytical gel includes only one protein. Rather, contamination by other proteins is more likely. Thus, in the case of all of the papers cited in this rejection, it is more likely that the proteins noted by the Office do not correspond to those of the present claims. They could easily be, rather, completely different proteins in the same size range or breakdown products of larger proteins. The Office has not even established their identity with the proteins and polypeptides of the present claims by probability, which still would not be sufficient to shift the burden of proof to applicant, as is discussed above.

Applicant also respectfully submits that the rejections under § 102 should be withdrawn, because the gels in each of the papers cited by the Office in supporting these rejections are analytical, not preparative, gels. What this means is that the amount of any particular protein present in a band on these gels is very low, and of course this amount would decrease further in any attempt to purify the protein from the gels. This would result, at best, in the isolation of a very, very small amount of protein that would be of no practical use.

Applicant further notes that, as is stated above, newly added claim 41 specifies that the protein of this claim is in "substantially purified form," a phrase that was present in the claims as

originally filed, and thus which has already been examined in this case. A protein is in a "substantially purified form," according to applicant's definition, if it is "separated from the medium in which it exists naturally" (page 3, lines 6-10 of the specification). The Office has in the past taken the position that this definition includes lysates, such as those described in the cited references, because such a form is not that which naturally occurs. As is discussed further below, applicants respectfully disagree with this interpretation of their definition.

To fully understand what is meant by applicant's definition, it is helpful to look at the definition in the context of the remainder of the teachings of the specification. A central focus of the specification is the description of methods for purifying *H. pylori* proteins of 54, 50, 32-35, or 30 kDa (see, e.g., pages 3-6 and 21-34), as well as methods for using these proteins in immunization methods. Indeed, the invention is based on the identification of these specific proteins and their use in these and other methods. Nowhere does the specification mention the use of lysates for any purpose other than as a source for purifying the specific proteins noted above. Thus, to conclude that applicant would intend to include lysates in their definition would be inconsistent with the teachings of the application as a whole, and thus applicant respectfully submits that those reading the application would clearly see that the phrase "substantially purified form" does not include within its scope lysates, such as those of the cited references. In view of this, applicant respectfully submits that claim 41 is also free of the prior art.

Applicant thus respectfully requests that the rejections in this case be withdrawn, and the present claims be allowed to issue.

CONCLUSION

Enclosed is a Petition to extend the period for replying to the Office Action for three months, to and including February 24, 2003 (February 23, 2003 fell on a Sunday), as well as a check in payment of the required fee. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095. In addition, in the event that any further issues remain in this case, applicants respectfully request that the Examiner contact the undersigned by telephone prior to taking any further actions on the merits.

Respectfully submitted,

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